Current Gene Therapy 2015 vol.15 N2, pages 266-276

Symptomatic improvement, increased life-span and sustained cell homing in amyotrophic lateral sclerosis after transplantation of human umbilical cord blood cells genetically modified with adeno-viral vectors expressing a neuro-protective factor and a neural cell adhesion molecule

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Abstract

© 2015 Bentham Science Publishers. Amyotrophic lateral sclerosis (ALS) is an incurable, chronic, fatal neuro-degenerative disease characterized by progressive loss of moto-neurons and paralysis of skeletal muscles. Reactivating dysfunctional areas is under earnest investigation utilizing various approaches. Here we present an innovative gene-cell construct aimed at reviving inert structure and function. Human umbilical cord blood cells (hUCBCs) transduced with adeno-viral vectors encoding human VEGF, GDNF and/or NCAM genes were transplanted into transgenic ALS mice models. Significant improvement in behavioral performance (open-field and grip-strength tests), as well as increased life-span was observed in rodents treated with NCAM-VEGF or NCAM-GDNF co-transfected cells. Active trans-gene expression was found in the spinal cord of ALS mice 10 weeks after delivering genetically modified hUCBCs, and cells were detectable even 5 months following transplantation. Our gene-cell therapy model yielded prominent symptomatic control and prolonged life-time in ALS. Incredible survivability of xeno-transpanted cells was also observed without any immune-suppression. These results suggest that engineered hUCBCs may offer effective gene-cell therapy in ALS.

Keywords

Adeno-virus, Amyotrophic lateral sclerosis (ALS), Gene-cell therapy, Glial cell-derived neuro-trophic factor (GDNF), Human umbilical cord blood cell (hUCBC), Human umbilical cord blood mono-nuclear cell (hUCB-MC), Neural cell adhesion molecule (NCAM), Vascular endothelial growth factor (VEGF), Viral vector